Carinal Forceps Biopsy Via the Fiberoptic Bronchoscope in the Routine Staging of Lung Cancer

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Main carinal biopsy was carried out in 58 consecutive patients with endobronchial (endoscopically visible) bronchogenic carcinoma. Overall, the results of the biopsy were positive in 8 of 58 patients (13.8%). The biopsy results were positive in 6 of 15 (40%) patients whose carina appeared abnormal as compared with 2 of 43 (4.7%) whose carina appeared normal (P = .0025). In those patients with subtle carinal abnormalities (carinal widening or erythema) but without gross tumor involvement, the biopsy findings were positive in 5 of 14 (36%). Unlike in previous studies, a significant percentage of positive carinal biopsy findings was associated with left upper lobe lesions. There were no complications associated with the procedure. Although the yield on blind carinal biopsies (visually normal carina) with the flexible fiberoptic bronchoscope is lower than that previously reported with the rigid bronchoscope, it remains a low-risk procedure that can spare a number of patients the morbidity and expense of more invasive surgical staging when applied as a routine part of diagnostic bronchoscopy in patients with endoscopically visible bronchogenic carcinoma.

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Accurate staging of bronchogenic carcinoma is important in determining resectability. A number of noninvasive methods have been recommended, but the lack of reliability of these techniques makes tissue confirmation mandatory.[1,2] Involvement of the main carina with mucosal or submucosal extension of an endobronchial carcinoma provides such tissue confirmation and, with rare exceptions, indicates unresectability because of the very poor prognosis associated with carinal involvement.[3,4]

A number of investigators have advised biopsy of the main carina as a routine staging procedure in patients with endoscopically visible bronchogenic carcinoma even when the carina appears normal (blind biopsy).[5-8] This recommendation is based on the finding of a significant proportion of positive results of blind carinal biopsy in patients with endobronchial carcinoma (10% to 42%).[6,8] Despite these findings, there is no evidence that routine carinal biopsy in the presence of an endobronchial tumor is a common practice today, even though the procedure may save a substantial number of patients the morbidity, mortality and expense of more invasive staging techniques.

Earlier studies showing a high yield with blind carinal biopsy were done using rigid bronchoscopes.[5-7] The only published study using a first-generation fiberoptic bronchoscope had a substantially lower yield.[8] We questioned whether this disparity was a result of disease extent at the time of initial bronchoscopy or of the different optical or biopsy capabilities of rigid bronchoscopes and first-generation flexible fiberoptic bronchoscopes. In this study we evaluate the usefulness of blind carinal biopsy as a routine staging procedure in patients with endobronchial carcinoma using a current-generation fiberoptic bronchoscope. Patients with peripheral lesions were not included in this study because previous investigators had found carinal mucosal involvement only with endobronchial carcinoma.[5,7]

Methods

In all, 58 consecutive patients who were found to have an endobronchial (endoscopically visible) lesion at the time of

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diagnostic bronchoscopy at the San Diego Veterans Administration Medical Center were entered in the study. After informed consent was obtained, the patients received atropine sulfate intramuscularly, meperidine hydrochloride intravenously and topical anesthesia with 0.45% tetracaine hydrochloride administered via an ultrasonic nebulizer. Bronchoscopy was done transnasally using an Olympus 1TR (2.6-mm channel) or an Olympus 4B2 (2-mm channel) bronchoscope. Separate forceps were used to do a biopsy of the primary endobronchial lesion and the carina. Large (2.2 mm) or regular (1.8 mm) fenestrated cup forceps were used depending on the size of the bronchoscope. At least three biopsy specimens were taken at each site, from the anterior tip, the posterior tip and the middle of the main carina. An attempt was always made to make the forceps biopsy deep enough to obtain submucosal tissue.

Before doing a biopsy of the carina, the bronchoscopist noted and characterized the appearance of the carina as normal or abnormal. An abnormal appearance was defined as gross tumor involvement (carinal involvement by the body of the tumor), widening of the carina or localized erythematous mucosal changes. The location of the primary lesion was also noted. The significance of differences between proportions was analyzed with the two-tailed Fisher's exact test.[9]

Results

A diagnosis of bronchogenic carcinoma was obtained in all 58 patients by biopsy of the primary endobronchial lesion. No complications occurred with biopsy of the primary lesion or of the carina.

The findings are summarized in Table 1. The results of the carinal biopsy were positive in 8 of the 58 patients (13.8%). The carina appeared to be abnormal by bronchoscopic examination in 15 patients and the biopsy specimen showed cancer in 6 of these 15 (40%). The carina appeared to be visually normal in 43 patients and the carinal biopsy specimen from 2 of the 43 patients (4.7%) contained cancer. The cancer in the eight positive carinal biopsy specimens included adenocarcinoma in three, squamous cell carcinoma in two, undifferentiated carcinoma in two and metastatic renal cell carcinoma in one. The difference between the proportion of positive results when the carina appeared normal versus abnormal is statistically significant ($P = .0025$).

TABLE 1.—*Results of Carinal Biopsy in 58 Patients*

Biopsy Findings	Carina Visually Abnormal No. of Patients	Carina Visually Normal No. of Patients	Total
Abnormal	6	2	8
Normal	9	41	50
Total	15	43	

TABLE 2.—*Relation of Primary Tumor Site to Positive Results on Carinal Biopsy*

Location	Positive Carinal Biopsies Number	Total Tumors Per Site Number	Percentage Positive Carinal Biopsies %
Left main stem	2	8	25
Right main stem	1	11	9
Left upper lobe	4	10	40
Right upper lobe	0	16	0
Left lower lobe	0	3	0
Right lower lobe	1	9	13
Trachea	0	1	0

Of the 50 patients who had normal biopsy results, two had small cell carcinoma and underwent no further staging, whereas seven were found to be inoperable at mediastinoscopy (tumor in paratracheal nodes). The remaining 41 underwent thoracotomy and surgical resection. The proximal margin of the resected bronchus was not found to be involved at the time of thoracotomy so the false-negative rate of carinal biopsy would appear to be low.

The distribution of tumor locations is shown in Table 2. The highest proportion of positive carinal biopsy results occurred with tumors on the left side (left main-stem and left upper lobe bronchi). The carinal biopsy findings were positive in 6 of 21 with left-sided tumors as opposed to 2 of 36 with right-sided tumors. This difference is statistically significant ($P = .042$).

Discussion

In 1945 Griess and co-workers[10] showed that significant microscopic spread of endobronchial carcinoma could occur proximal to the gross visible limits of an endobronchial tumor without producing overlying mucosal changes. This microscopic spread occurs mainly in the mucosal and outer fibrous layers of the bronchus, though tumor can also spread along the submucosal layer. When this proximal extension involves the main carina, surgical options are limited. The extensive surgical resection necessary for cure is associated with a high operative mortality and poor long-term survival and is rarely, if ever, indicated.[3,4]

The significance of microscopic spread of bronchogenic carcinoma with respect to doing a blind biopsy of the carina was later documented by Rabin and associates,[5] who found a 10.4% incidence of positive findings on blind carinal biopsies done via the rigid bronchoscope in 154 patients. The population of patients undergoing carinal biopsy in their study included patients with peripheral (not endoscopically visible) lesions and those with endobronchial lesions. Because carinal biopsy specimens never showed abnormalities in patients with peripheral lesions, the percentage of positive blind biopsies in the appropriate patient group (endobronchial lesions) was actually much higher. Waltner[6] later confirmed this result in a smaller group of patients (12), finding cancer on blind carinal biopsy in 42% of his patients. Versteegh and Swierenga[7] found a 13% positive rate also using a rigid bronchoscope. Robbins and colleagues[8] found a substantially lower rate of blind carinal biopsies (6%) but showed the feasibility of carinal biopsy through the fiberoptic bronchoscope.

The findings of our study, using the latest generation of fiberoptic bronchoscopes, agree with the results obtained by Robbins and co-workers.[8] We found a similar incidence of positive results on carinal biopsy overall (13.8% versus 10%), and a similar incidence of positive results on blind carinal biopsy (4.7% versus 6.0%). The carinal abnormalities noted in this study, like those seen by Robbins and colleagues,[8] were mostly the more subtle ones of carinal widening or mucosal erythema. Gross tumor involvement was seen in only one patient. Whether the difference in results

obtained with fiberoptic bronchoscopy and rigid bronchoscopy is due to different optical or biopsy capabilities of the instruments or to more advanced disease in the latter series at the time of initial bronchoscopy remains uncertain. Whatever the reason, the significance of these results seems clear. Carinal biopsy done at the time of initial bronchoscopy in patients with endobronchial carcinoma is capable of identifying a subgroup of patients with unresectable disease. Additional staging procedures, with their attendant morbidity and risk, become unnecessary.

It is also evident that a visually abnormal carina does not necessarily predict tumor involvement unless such involvement is extensive. In our series, 64% of those with subtle carinal abnormalities had true-negative results on biopsy. This finding is in agreement with the results obtained by Robbins and associates,[8] in which 80% of subtle carinal abnormalities proved not to be a result of tumor extension.

Our results differed from those of previous studies in the relation between a positive finding on carinal biopsy and the location of the primary tumor. Others[5,6,8] have found the majority of carinal biopsies with positive findings to be associated with primary lesions in the main-stem bronchi (left and right), followed by right-sided lobar primary lesions. Rabin and Robbins and co-workers[5,8] found no abnormalities on carinal biopsy when the primary lesion was located distal to the left main-stem bronchus, although Waltner[6] reported one case showing positive findings on carinal biopsy with an associated left upper lobe lesion. In contrast to these earlier studies, we found the majority of positive results on carinal biopsy to be in association with left-sided tumors and particularly with left upper lobe tumors in which the carinal biopsy specimen contained malignant tumor in 40%. We do not know the reason for this difference, but, considering all the studies together, it suggests that tumor location may not be a meaningful factor in the incidence of positive results on carinal biopsy. It does appear, however, that the distance between the primary lesion and the carina influences the yield of carinal biopsy. Combining the series of Robbins and colleagues[8] with our own, lesions in the main-stem bronchi had an incidence of positive findings on carinal biopsy of 21%; those in the upper lobe bronchi, 10%, and those in the lower lobe bronchi, 5%. Abnormalities on the carinal biopsy specimen have not been found in patients with peripheral (not endoscopically visible) tumors. Because carinal involvement appears to occur by direct extension along one or more layers of a bronchus, it is not surprising that peripheral lesions involve the carina less frequently.

Although the biopsy specimen of a visually abnormal carina is much more likely to show tumor involvement than that of a visually normal carina, the procedure is a low-risk one, without reported complications, and may still spare a small but meaningful number of patients more invasive surgical staging. If the procedure were applied at the time of initial bronchoscopy to the estimated 54,000 new cases of endobronchial carcinoma occurring annually,[11] 7,500 patients would be spared further surgical staging.

Forceps biopsy of the carina, which assesses mucosal or submucosal tumor involvement, does not replace transcarinal needle aspiration for staging the subcarinal nodes.[12,13] Tumor can spread from an endobronchial site to the carinal mucosa or submucosa without involving the subcarinal nodes; conversely, tumor can be present in subcarinal nodes without involving the overlying carinal mucosa.

We conclude that carinal biopsy is a low-risk procedure that should be done in patients with endobronchial lesions, particularly in those whose carina appears abnormal. Because most of the carinal abnormalities were subtle ones, some of which may be missed through interobserver variation, and because the yield with blind biopsy was small but not insignificant, carinal mucosal biopsy should probably be done in all patients with endobronchial carcinoma as a routine staging procedure, regardless of carinal appearance or endobronchial tumor location.

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